

# Improving economic evaluations in stroke: a report from the ESO Health Economics Working Group

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## **Abstract (250 word limit)**

**Introduction:** Approaches to economic evaluations of stroke therapies are varied and inconsistently described. An objective of the European Stroke Organisation (ESO) Health Economics Working Group is to standardise and improve the economic evaluations of interventions for stroke.

### **Methods:**

The ESO Health Economics Working Group and additional experts were contacted to develop a protocol and a guidance document for data collection for economic evaluations of stroke therapies. A modified Delphi approach, including a survey and consensus processes, was used to agree on content. We also asked the participants about resources that could be shared to improve economic evaluations of interventions for stroke.

**Results:** Of 28 experts invited, 16 (57%) completed the initial survey, with representation from universities, government, and industry. More than half of the survey respondents endorsed 13 specific items to include in a standard resource use questionnaire. Preferred functional/quality of life outcome measures to use for economic evaluations were the modified Rankin Scale (14 respondents, 88%) and the EQ-5D instrument (11 respondents, 69%). Of the 12 respondents who had access to data used in economic evaluations, 10 (83%) indicated a willingness to share data. A protocol template and a guidance document for data collection were developed and are presented in this manuscript.

**Conclusion:** The protocol template and guidance document for data collection will support a more standardised and transparent approach for economic evaluations of stroke care.

**Key words:** stroke, economic evaluation, health policy, health outcomes, modified Rankin Scale, EuroQol

## **Introduction**

Interventions for stroke need to be evaluated for their cost-effectiveness, as well as their clinical effectiveness. Several countries now incorporate results of health-economic analyses as part of their national clinical guidelines for stroke.<sup>1,2</sup> A paucity of published cost-effectiveness studies means that very few clinical recommendations in these guidelines have information about the value of treatments. Comparability and translation of economic evaluation results are complicated by variability of study methods and differences in health care system organization and expenditure across national and regional settings.<sup>3</sup> Another limitation is that the quality of studies varies between studies.<sup>4</sup> Therefore, with the growing number of interventions becoming available to prevent or treat stroke, it is important to standardise and improve the methods for conducting cost-effectiveness studies in stroke.

While checklists exist for the reporting of economic evaluations, no guidance is provided regarding collection of data on resource use or costs. In addition, existing recommendations for health-related economic evaluations are generic and do not provide guidance specifically for research related to patients with stroke. The European Stroke Organisation (ESO) Health Economics Working Group had its first meeting in 2015 to discuss the standardisation of health economic methods for future clinical trials,<sup>3</sup> and was formally established in 2016 with broad aims of compiling and developing resources to facilitate economic evaluations of stroke therapies (Table 1). In this manuscript, we give recommendations for a more standardised and transparent method for economic evaluations of stroke care.

## **Methods**

The ESO Health Economics Working Group was established in 2015 after discussion among 53 ESO members who had experience with economic evaluations of stroke therapies. Of the

53 experts, 10 were nominated as members of the executive group, while a further 14 were retained as corresponding members.

The working group used a modified Delphi technique for the present project.<sup>5</sup> At the annual meeting at the ESO Conference in Prague in 2017, the participants agreed on a survey, which was distributed to 28 experts in economic evaluations of stroke therapies, including the members of the ESO Health Economics Working Group. The core questions in the survey focused on protocols for economic evaluations and the data collected for economic evaluations (see Online Supplement). The survey also included questions about resources that could be shared to improve economic evaluations in stroke research, including access to existing datasets and models used for economic evaluations.

Based on the responses from the survey, a protocol template and a guidance document for data collection were developed. These materials were further refined prior to presentation at the annual meeting at the ESO Conference in Gothenburg in 2018, where the materials were reviewed and consensus on the content was reached by the working group.

## **Results**

The survey was sent to the 26 working group members and two other researchers nominated by the working group for their specific expertise. Of the 28 people invited to participate in the survey, 16 responded, of which seven worked at universities or hospitals, two in government, two in industry and five did not provide their affiliations or occupation.

### *Use of standard protocols*

Of the 16 respondents, 13 did not use a standard template for economic evaluation protocols (81%). However, five (31%) used a checklist to guide the development of their protocols. Respondents used the Consolidated Health Economic Evaluation Reporting Standards (CHEERS),<sup>6</sup> the Drummond checklist<sup>7</sup> and the National Institute for Health and Care Excellence (NICE) guidelines for England to guide development of protocols.<sup>8</sup> The protocol items suggested by the respondents are outlined in Figure 1.

### *Use of questionnaires to capture resource use*

Fifteen respondents did not have a standard resource use questionnaire for economic evaluations (94%). Respondents indicated their support for items to be included in a standard questionnaire to capture resource use (Figure 2). At least 50% of respondents supported inclusion of 13 suggested items for a standard resource use questionnaire. Other suggested items compiled from the open text responses were: outpatient procedures, diagnostic tests, transport between hospitals, distance to care provider, and income. When asked about the level of detail required for the data collected, it was suggested that when collecting information about consultations/services provided by health professionals, the number of consultations, type of provider, duration, and out-of-pocket costs were important. When collecting information about medications, it was suggested that researchers could collect the broader categories of medications used by patients (e.g. antihypertensive, antithrombotic). The importance of tailoring the data collection was emphasised, and it was suggested that the amount of detail collected should depend on whatever helps to quantify the important drivers of cost relevant to that study.

### *Estimating resource use from routinely collected data*

The majority of respondents indicated that they estimated resource use based on stroke type (n=11, 69%), discharge destination (n=10, 63%) or by first ever or recurrent stroke (n=9, 56%). Other clinical or demographic data that could be used to estimate resource use included time since stroke, modified Rankin Scale<sup>9</sup> (mRS) at discharge and 90 days, age, sex, comorbidities (e.g. atrial fibrillation) and the National Institute of Health Stroke Scale<sup>10</sup> (NIHSS) score.

### *Patient outcomes*

The most popular outcome measure for economic evaluations of stroke therapies were the mRS<sup>9, 11</sup> (n=14, 88%) followed by the EQ-5D instrument<sup>12</sup> (n=11, 69%). Other outcome measures included the Stroke Impact Scale,<sup>13</sup> Assessment of Quality of Life<sup>14</sup> (AQoL) and the Barthel Index.<sup>15, 16</sup> All respondents indicated that they collected the mRS as an ordinal scale. An advantage of the mRS was having published literature on the direct costs for each category which is useful for studies where it has not been possible to collect data on resource utilisation/costs directly from participants. An advantage of health-related quality of life measures, like the EQ-5D and the AQoL, is that they can generate utility values that can directly enter into calculations of quality-adjusted life years (QALYs). The mRS and Barthel Index can be converted to utility values to serve this purpose, although the assigned utility scores are less granular than with direct quality of life measures.<sup>17, 18</sup>

### *Sharing available resources and data for economic evaluations*

There were 11 respondents (69%) who indicated that they had access to datasets used for economic evaluations. The scope of data was broad and included data from clinical trials (acute, subacute and community-based intervention studies), administrative data, national registry data or cost data.

Of the 11 respondents who had access to existing economic evaluations data, 9 (82%) replied that they were willing to share data and 9 (90%, 1 missing response) indicated that permission to use the data would be needed, as well as funding to cover any administrative expenses (e.g. formatting the data). The issue of needing ethical approvals for secondary use of the data and the importance of acknowledging the original source of the data was expressed.

### *Models for economic evaluations*

The short duration of clinical trials and the long term consequences of stroke renders modelling almost inevitable since economic evaluations based upon trial results would not capture fully the benefits or harms of interventions. Eight of the respondents (50%) indicated that they had previously used models for economic evaluations, including Markov models, partition survival modelling and discrete event simulation. Several were developed in Microsoft Excel with and without add-on software and with different levels of sophistication (Visual Basic for Applications coding). The use of software such as TreeAge, SAS, R and Stata for developing models was also mentioned.

### *Final protocol template and guidance document for collecting resource use and cost data*

Table 2 includes the items that were agreed for a protocol template for economic evaluations of stroke therapies, and Table 3 includes information to guide data collection on resource use. In Table 3 we highlight the importance of estimating the additional costs of the intervention, which would include items such as the cost of therapists and support staff, training and education, equipment, medication or facility costs. Estimating the costs of the intervention may be complex, and this must be considered in the data collection. For example, the costs of a novel treatment with a large capital outlay may be more obvious than subtle adaptations to



existing care pathways. It was noted that evidence from process evaluations would assist with informing the costs to include.

## **Discussion**

In this article, we have presented a consensus-based protocol template and a guidance document for the collection of resource use data that can be used for economic evaluations of stroke therapies internationally. We recommend using these tools in addition to the generic guidelines for conducting and reporting economic evaluations. To support use in practice, two examples of economic evaluations of stroke therapies that have been summarised using our protocol template have been provided in the online supplement and Supplemental Table I.

In addition to the resources we have developed to improve the quality of economic evaluations of stroke interventions, participants supported the collection of information that will enable comparison of studies. Providing information on case mix and stroke severity of participants (e.g. the National Institute of Health Stroke Scale scores) would also assist with comparison between economic evaluations. Researchers should also consider reporting information on the structure of healthcare systems and hospitals, particularly for multi-country studies. In intensive care studies, the Therapeutic Intervention Scoring System (e.g. TISS-28) is recommended as a way to standardise costs between countries.<sup>19</sup> A similar tool for stroke care could be developed for stroke as an extension of our current work. In the A Very Early Rehabilitation Trial (AVERT), the data collection instruments were tailored to different study centres in Australia, Asia and the United Kingdom.<sup>20</sup> Reporting cost base years, currencies, inflation indices/rates and currency exchange indices/rates is recommended in generic guidelines for reporting economic evaluations. Adhering to this recommendation would permit

researchers to assess the comparability and generalisability of economic evaluations across settings.

Standardising the time horizons and perspectives would also assist with comparison of results. When conducting studies using long-term time horizons, results for shorter-term time horizons could also be reported. The perspectives of studies are often limited to direct inpatient costs (hospital or rehabilitation) although post-hospital healthcare (community) and societal costs (broader than just the health sector impacts) are as important. The costs of long-term care and support are also important, especially in evaluations of interventions that affect disability after stroke. For example, early after stroke, hospitalisation and rehabilitation would be considered as essential since these are major contributors to costs in the first year after stroke.<sup>21, 22</sup> In the longer-term, there is evidence that residential aged care facilities and informal care comprise the majority of costs.<sup>23, 24</sup> Therefore, we recommend researchers report the type of costs incurred (e.g. hospital, community health services, gains/losses to productivity) and the time point at which these costs were incurred. For longer term economic evaluations societal costs must be captured to have meaningful results. Effects on household productivity (e.g. cooking, cleaning, gardening and caring for family members) may also be considerable in older cohorts or for women,<sup>25</sup> but this is typically overlooked in health technology assessments. Reporting informal care quantities, valuation approaches and costs are recommended to enable alternative valuations to be estimated if necessary. In other fields, questionnaires that can be used to collect indirect costs (carers' time and indirect consequences on carers' health) have been validated.<sup>26</sup>

Participants acknowledged that a comprehensive economic evaluation may require multiple overlapping data collection methods to be used. This could include direct measurement of healthcare resource use from registries or hospital billing systems to allow for standardised

capture of all given care, a detailed evaluation of workforce time spent with the patient to add accuracy to measuring a specific care component, and the administration of patient/caregiver questionnaires to collect data on informal care, lost productivity and any health or social care resource use (societal costs) which is not accessible from routine records. The possibility of data linkage for the purposes of economic evaluations should be explored given there are inaccuracies with self-reported data and the potential for recall bias especially when there are long delays in between follow-up assessments.<sup>22</sup> Ideally, data collected to estimate costs should be traceable to routinely collected information in registries and administrative databases. Information about resource use prior to stroke can also be obtained through data linkage in order to quantify stroke-specific costs (i.e. increase in resource use after stroke). In addition, data linkages with clinical quality registries can make it possible to obtain patient reported outcomes at routine follow-up assessments. For example, by linking to the Australian Stroke Clinical Registry mRS and health-related quality of life using the EuroQol-5 dimension-3 level questionnaire collected at 90 and 180 days after stroke would be available.<sup>27</sup> However, the time delays in obtaining linked data and their complexity to analyse needs careful consideration when planning studies.<sup>28</sup>

The participants recognised the potential value of having data repositories or directories of data custodians and existing protocols, datasets, questionnaires and models that might be shared and adapted. Once available, having access to these resources will expedite economic evaluations of stroke therapies and facilitate comparability between studies. Processes to seek permission to access these resources, in compliance with relevant information governance legislation and frameworks, remain to be developed. However, improved accessibility is likely to emerge over time from wider movements towards open access to research data.

Our process for achieving the outcomes of this work in seeking to improve economic evaluations undertaken within the field of stroke may be an exemplar for other speciality fields within health. We acknowledge that in the final review we took a pragmatic approach to finalise the outstanding decisions within the executive committee, and this may be considered a limitation of the consensus process.

### **Summary**

The ESO Health Economic Working Group aims to standardise and improve the methods of health-economic evaluations of stroke therapies. The resources that were developed and presented in this paper will facilitate these aims and ultimately contribute to the development of evidence-based clinical guidelines to improve patient care.

### **Acknowledgements**

Helen Dewey for contribution to the working group.

**Table 1. Actions suggested for the working group**

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**Compiling existing resources for economic evaluation**

1. Develop a directory of health-economic models, protocols and questionnaires
2. Investigate processes required to identify and share such resources
3. Identify manuals for health technology assessment in each country

**Development of resources for the standardisation of economic evaluations**

1. Develop a protocol template for health-economic evaluations in stroke
  2. Develop a common model
  3. Develop a data collection questionnaire template with recommendations for essential, recommended and elective categories of variables
  4. Develop recommendations on how data should be systematically collected
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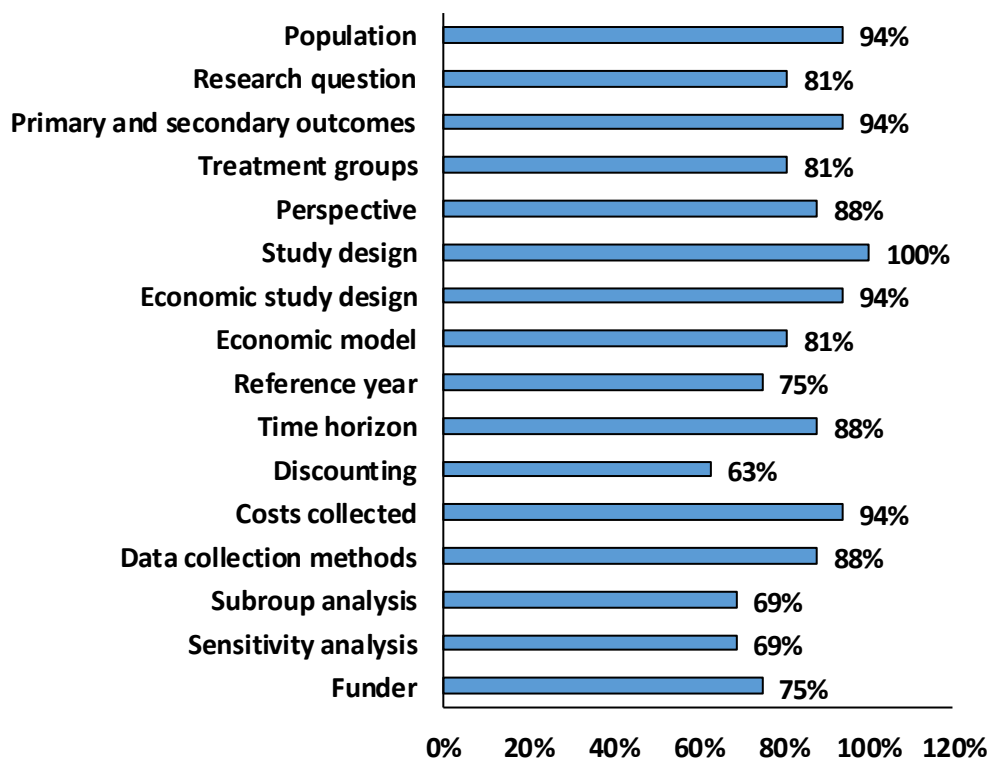
**Table 2. Protocol template**

<b>Item</b>	<b>Detail required or examples</b>
<b>Population and setting</b>	Country/region Sub-groups of patients with stroke Organisational structure (private/public) Care pathways
<b>Research question</b>	E.g. to determine/estimate the cost-effectiveness of intervention compared to comparator/control group
<b>Outcomes</b>	The outcome that is used for the cost-effectiveness measure Questionnaire used to estimate quality of life
<b>Treatment groups</b>	Intervention groups Comparator/control groups
<b>Perspective</b>	Health service Patient Societal Direct/indirect
<b>Study design / data source</b>	Alongside RCT Model-based economic evaluations using data from multiple sources
<b>Economic study design</b>	Cost benefit Cost effectiveness Cost utility Budget impact analysis
<b>Economic model</b>	E.g. model assumptions, model name and reference in literature
<b>Reference year</b>	E.g. Year and inflation/deflation. Source for adjusting costs
<b>Time horizon</b>	Assumptions made for modelling longer-term costs and outcomes
<b>Discounting</b>	Nationally recommended – usually 3% or 5%
<b>Resource use collected</b>	E.g. Hospital readmissions, family physician contacts <ul style="list-style-type: none"> <li>• Delivery of the intervention and justification for inclusion</li> <li>• If used, the method of estimating resource use based on clinical or demographic details of participants and the reference in literature</li> </ul>
<b>Data collection methods</b>	Administrative data Patient self-report via survey
<b>Sub-group analysis</b>	Stroke type Hospital type (private/public)
<b>Sensitivity analysis</b>	Monte Carlo simulation (multivariable) One-way sensitivity Scenario analysis
<b>Funder</b>	Government Industry Private insurance

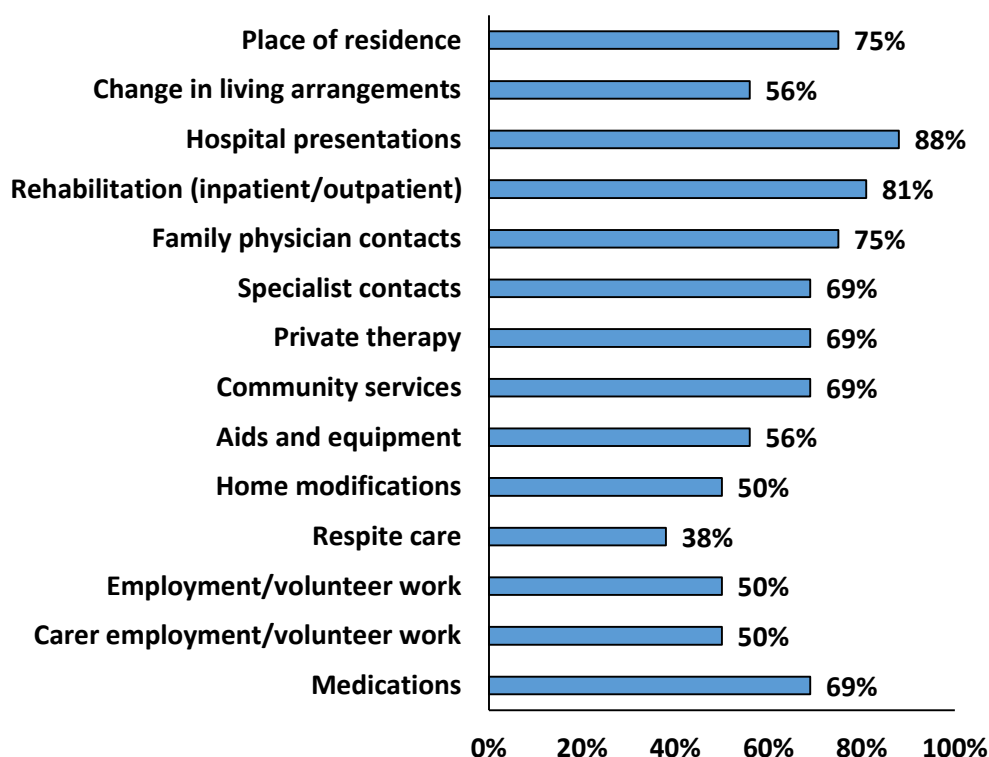
**Table 3. Resource use data collection guidance**

Variables	Data collection guidance
<b><u>Additional costs of treatment</u></b>	This should be the costs of delivering the new treatment that are above and beyond a comparator treatment or usual care
<b><u>Data collection to be considered for studies using a health care sector perspective*</u></b>	
<b>Transport</b>	Transport between hospital (e.g. transfer to a centre providing reperfusion) or from home, type of vehicle
<b>Rehabilitation</b>	Inpatient or outpatient rehabilitation, number of sessions, length of stay, specific services and procedures provided while in rehabilitation (e.g. assessment of impairment)
<b>Hospital presentations</b>	Number of presentations, type of presentation (e.g. emergency department or admission), dates or length of stay, specific services and procedures provided while in hospital (e.g. reperfusion)
<b>Respite care</b>	Number of times used, length of stay
<b>Medications</b>	Type of medications (e.g. antihypertensive medications), number of medications, dose, time on medication
<b>Change in residence and living arrangements</b>	Information to capture changes in residence as this is an indicator of independence that affects costs (e.g. costs of moving to an aged care facility may be applied)
<b>Home modifications</b>	Type of home modifications and out-of-pocket costs (e.g. for the installation of ramp to home)
<b>Aids and equipment</b>	Type of aids and equipment and out-of-pocket costs (e.g. for a walking frame)
<b>Community services</b>	Type of service, number of times provided and out-of-pocket costs
<b>Family physician contacts</b>	Number of contacts, other associated services (e.g. practice nurse) and out-of-pocket costs
<b>Specialist contacts</b>	Type of specialist, number of contacts and out-of-pocket costs
<b>Private therapy</b>	Type of therapy, number of contacts and out-of-pocket costs
<b>Diagnostic tests</b>	Type of tests, number of tests and out-of-pocket costs
<b><u>Data collection to be considered for studies using a societal perspective</u></b>	
<b>Employment/volunteer work</b>	Type of work and hours, income and change since stroke
<b>Carer employment/volunteer work</b>	Type of work and hours, income and change since stroke
<b>Household productivity</b>	Type of activity and hours and change since stroke (e.g. cleaning, cooking, gardening, caring for family members)
<b>Leisure time</b>	Type of activity and hours and change since stroke
<b><u>Additional items to consider</u></b>	
<b>Clinical assessments at baseline</b>	These should be clinical assessments that can be used to estimate costs (e.g. modified Rankin Scale)
<b>Clinical outcomes after treatment</b>	These should be clinical assessments that can be used to estimate costs (e.g. modified Rankin Scale)

\* Collecting data on the utilisation of health services can be labour intensive. Limiting data collection to certain categories of resource use and types of resources should be justified.



**Figure 1. Support for the inclusion of items in a standard health-economic evaluation protocol in stroke**



**Figure 2. Support for the inclusion of suggested items on a standard resource use questionnaire in stroke**



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## Online Supplement

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## **Online Supplement**

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### **ESO HEWG Survey Questions**

#### **PROTOCOLS**

**1) Do you have a standard protocol for economic evaluations?**

[Yes / No]

**If yes, - 1b) Would you be willing to share your protocol or summary of a protocol?**

[Yes / No]

**1c) Would others need permission to use it?**

[Yes / No]

[free text]

**2) Indicate standard headings that you believe should be included in an economic protocol**

[Tickboxes]

- Population
- Research question
- Primary and secondary outcomes
- Treatment groups
- Perspective (E.g. societal, health-care system)
- Study design (E.g. parallel to RCT, simulation model)
- Economic study design (E.g. cost-utility analysis)
- Economic model
- Reference year
- Time horizon
- Discounting
- Costs collected
- Data collection methods
- Subgroup analysis
- Sensitivity analysis
- Funder

**3) What other information should be provided in a protocol for an economic evaluation?**

[free text]

**4) Is the information you provide on a protocol guided by a checklist or framework?**

[Yes / No]

**If yes, - 4b) State the checklist or framework**

[free text]

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### RESOURCE USE DATA

**5) Do you have a standard resource-use questionnaire for economic evaluations?**

[Yes / No]

**If yes, - 5b) Would you be willing to share the standard resource-use questionnaire template?**

[Yes / No]

**5c) Would others need permission to use it?**

[Yes / No]

[free text]

**6) What do you think are important data that should be captured on a standard resource use questionnaire?**

[Tickboxes]

- Place of residence
- Change in living arrangements
- Hospital presentations
- Rehabilitation (inpatient/outpatient)
- Family physician contacts
- Specialist contacts
- Private therapy
- Community services
- Aids and equipment
- Home modifications
- Respite care
- Employment/volunteer work
- Carer employment/volunteer work
- Medications

**7) What other resource-use information should be captured on a resource use questionnaire?**

[free text]

**8) What level of detail is captured for these items on the resource use questionnaire (E.g. number of contacts, duration of contacts, out-of-pocket costs)?**

[free text]

**9) Are there routinely collected clinical/demographic data that should be used to estimate resource use?**

[Tickboxes]

- First ever or recurrent stroke
- Stroke type
- Discharge destination

**10) What other routinely collected clinical/demographic data should be collected for estimating resource use?**

[free text]

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### **PATIENT-REPORTED OUTCOME MEASURES**

**11) Which patient reported outcome measures do you collect for economic evaluations?**

- SIS
- Modified Rankin Scale
- EQ-5D-3L
- AQoL
- Other (please specify)

**12) If you collect the modified Rankin Scale, is it collected as an ordinal scale?**

[Yes / No]

### **EXISTING DATASETS**

**13) Have you collected or do you have access to any data used in economic evaluations (e.g. patient-level cost data)?**

[Yes / No]

If yes,

**14) Please describe the dataset:**

[free text responses]

**15) What was the purpose of the data when originally collected?**

[free text]

**If yes, - 15b) Would you be willing to share the data?**

[Yes / No]

**15c) Would others need permission to use it?**

[Yes / No]

**16) What is the perspective of the data collected?**

- Hospital/health service
- Government
- Societal
- Private
- Patient

**17) What is the structure and format of the data (e.g. Microsoft Excel)?**

[free text]

**18) Please provide any publications where the data are reported**

[free text]

### **ECONOMIC MODELLING**

**19) Have you used modelling for economic evaluations?**

[Yes / No]

**20) What kind of model and what software was used for the creation of this model?**

[free text]

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### **HEALTH TECHNOLOGY ASSESSMENT**

**21) Does your country have specific costing guidelines for health technology assessment or other purposes?**

[Yes / No]

If yes,

**22) Please provide a reference or URL**

### **STROKE GUIDELINES**

**23) Does the stroke clinical guideline in your country include information about economic evaluations supporting the recommendations?**

[Yes / No]

If yes,

**24) How is this incorporated in the guidelines?**

**25) Please provide a reference or URL**

**26) Please provide any other general comments regarding the survey**



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### **Detailed methods and timeline for establishing agreement on a protocol template and guidance document for data collection**

We used a modified Delphi technique which is a method for consensus-building with a group of experts whereby an initial questionnaire is used as the basis for obtaining responses which are then summarised and fed back to participants.<sup>1</sup> The most important first step is choosing appropriate participants because this directly relates to the quality of the results generated.<sup>1</sup> The ESO Health Economics Working Group was established via a process of identifying experts or their nominees associated with the ESO who were publishing relevant papers, including industry. An initial group of 53 experts were identified to be potential members of the working group and 10 agreed to be Executive members of the working group (DAC nominated as Chair), while a further 14 were retained as corresponding members. JK and AW were included in the working group as coordinators. The Executive committee was responsible for driving the work program including for this project.

The following process was undertaken to achieve consensus for a protocol template and a guidance document for data collection that could be used to improve the standard of economic evaluations of stroke interventions. Proposed questions for a survey were developed by DAC, JK and AW and presented to 20 members of the working group at the annual meeting at the European Stroke Conference 2017 held in Prague (17/05/2017). Proposed questions were refined into a survey by DAC, JK and AW via email discussions (21/05/2017) and distributed to 26 members of the working group on 11/07/2017. The core questions in the survey focused on protocols for economic evaluations and the data collected for economic evaluations (resource use items included in questionnaires and patient-reported outcome measures) (see Online Supplement). The survey also included questions about resources that could be useful

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to improve economic evaluations of stroke therapies, including access to existing datasets and models used for economic evaluations.

The survey was closed on 16/08/2017 after recipients were given a final reminder on 02/08/2017. Initial survey results were analysed by JK and presented to DAC and AW via email correspondence and a teleconference (09/11/2017). The results of the survey were then discussed during a teleconference with available Executive working group members (n=8) on 27/11/2017. A protocol template and guidance document for data collection were developed based on the survey results. These materials were further refined based on the feedback from the working group by DC and JK and discussed via email (08/04/2018) and a teleconference (24/04/2018) with AW prior to presentation at the annual face to face meeting at the European Stroke Conference 2018 held in Gothenburg, 16/05/2018. The meeting was attended by 9 members of the working group. The draft materials were reviewed, and consensus reached. It was agreed that a manuscript would be prepared as a method for ensuring all working group members contributed to the final scope and presentation of the protocol template and guidance document.

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### Protocol summaries of case studies

The Very Early Rehabilitation of Speech (VERSE) trial<sup>2</sup> used standardised questionnaires to collect resource use, and validated questionnaires to collect information on outcomes at routine follow-up assessments conducted at 12 and 26 weeks after stroke. The resource use data collected will enable an economic evaluation from both a societal and health sector perspective at a time horizon of 26 weeks. When there is an absence of data obtained directly from participants and/or the healthcare system, simulation modelling using a range of ‘best available’ data may be required. In the economic evaluation by Sandercock et al.,<sup>3</sup> a decision analytic model was used to determine the cost-utility of thrombolytic treatment for acute ischaemic stroke from the perspective of the United Kingdom’s National Health Service at a 1-year and a lifetime time horizon. Markov modelling was used after the first year. The patient population was based on data obtained for a stroke registry, effectiveness estimates of thrombolysis were taken from a Cochrane systematic review, utility values for each health state were obtained from published literature, and costs were obtained from health services in the United Kingdom and from published literature.

### Supplemental table I Case study examples

	<b>A Very Early Rehabilitation in Speech (VERSE) Trial</b>	<b>Sandercock et al, 2004</b>
<b>Population and setting</b>	Patients with acute stroke and aphasia at acute care hospitals and accompanying rehabilitation services throughout Australia	Acute stroke patients admitted to hospital from the Lothian Stroke Register in England
<b>Research question</b>	To determine the cost-effectiveness of an intensive prescribed aphasia therapy compared to non-prescribed and non-intensive aphasia therapy	To estimate the cost-effectiveness of thrombolytic treatment in the UK National Health Service
<b>Outcomes</b>	Cost per 4.4% improvement on the aphasia quotient	Cost per quality adjusted life year gained Estimates of quality adjusted life years gained were obtained directly from patients in the Lothian Stroke Register
<b>Treatment groups</b>	<ul style="list-style-type: none"><li>Intensive prescribed aphasia therapy (VERSE)</li></ul>	<ul style="list-style-type: none"><li>Standard care</li><li>Standard care plus thrombolysis</li><li></li></ul>

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	<ul style="list-style-type: none"> <li>• Non-prescribed, intensive aphasia therapy (usual care-plus)</li> <li>• Non-intensive usual care aphasia therapy (usual care)</li> </ul>	
<b>Perspective</b>	Societal with the main focus on the health sector, including out-of-pocket costs and productivity	Broad health care and personal social services perspective
<b>Study design / data source</b>	Resource use collected from a randomised controlled trial	<p>Decision analysis model (until 1 year time horizon) and a Markov modelling approach (lifetime time horizon) using published literature and data collected from the Lothian Stroke Register.</p> <ul style="list-style-type: none"> <li>• Published literature and data on treatment and outcomes from the Lothian Stroke Register,</li> <li>• Published literature for effectiveness estimates of thrombolysis and outcomes</li> <li>• Unit cost information obtained from health services</li> </ul>
<b>Economic study design</b>	Cost-effectiveness	Cost utility
<b>Economic model</b>	N/A	Original decision analysis model, but costs of rehabilitation and long-term care obtained from the MEDTAP model.
<b>Reference year</b>	2017, with adjustments between years made using the Total Health Price Index published by the Australian Institute of Health and Welfare	Not stated
<b>Time horizon</b>	26 weeks	1 year and lifetime
<b>Discounting</b>	N/A	6%
<b>Resource use collected</b>	<ul style="list-style-type: none"> <li>• Hospital presentations (emergency department presentation and hospital admissions)</li> <li>• Rehabilitation (inpatient and outpatient)</li> <li>• Residential aged care</li> <li>• Ambulance transfers</li> <li>• GP services</li> <li>• Rehabilitation services provided at home</li> <li>• Community services</li> <li>• Speech aids and equipment</li> <li>• Private speech therapy sessions</li> <li>• Respite care</li> <li>• Employment</li> <li>• Informal care provided</li> <li>• Therapist time</li> </ul>	<ul style="list-style-type: none"> <li>• Thrombolysis drug costs</li> <li>• Length of stay in hospital</li> <li>• Rehabilitation</li> <li>• Long-term care</li> <li>•</li> </ul>

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<b>Data collection methods</b>	Standardised resource use questionnaire administered at 12 weeks and 26 weeks	From published sources
<b>Sub-group analysis</b>	No	No
<b>Sensitivity analysis</b>	Monte Carlo simulation	<ul style="list-style-type: none"><li>• One-way sensitivity analysis</li><li>• Threshold analyses</li><li>• Monte Carlo simulation</li></ul>
<b>Funder</b>	National Health and Medical Research Council	National Health Service

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### **References**

1. Hsu C-C, Sanford BA. The Delphi Technique: Making Sense Of Consensus Practical Assessment, Research & Evaluation 2007;12:1-8.
2. Godecke E, Armstrong EA, Rai T, et al. A randomized controlled trial of very early rehabilitation in speech after stroke. International Journal of Stroke 2016;11:586-592.
3. Sandercock P, Berge E, Dennis M, et al. Cost-Effectiveness of Thrombolysis With Recombinant Tissue Plasminogen Activator for Acute Ischemic Stroke Assessed by a Model Based on UK NHS Costs. Stroke 2004;35:1490-1497.